Fetal Magnetoencephalography (fMEG)

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Contents

Abstract

The human brain is one of the most complex organs which develops and adapts continuously over lifetime. Until now, neurophysiological research is mainly

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related to brain development from birth to adulthood, and neurophysiological research concerning prenatal human brain development only started in the last decades. Magnetoencephalography (MEG) is especially suited for fetal investigation, because it is completely noninvasive and not affected by the biological tissue separating the fetus from the outside. The first successful fetal MEG (fMEG) recording was reported in 1985 (Blum et al. Br J Obstet Gynaecol 92(12):1224–1229, 1985). Since the human brain in utero is highly vulnerable to internal and external influences, prenatal brain research is highly important to understand its development during that time period. Therefore, measurement techniques were improved, and basic research concerning brain development in utero was conducted. So far, mainly auditory and visual stimulation was used to assess fetal brain development by means of changes in signal processing speed or the development of basic forms of learning. The goal of basic fMEG research is to understand healthy fetal brain development and enable an early detection of possible deviations from it. In the future this may allow the development of early, even prenatal treatments and reduce the risk of adverse outcomes. This chapter gives an overview over structural and functional brain development and introduces the fMEG, a measurement technique to noninvasively assess functional fetal brain development in utero. Moreover, current fMEG studies are introduced, and the potential of the method of fMEG is illustrated and discussed.

Keywords
Auditory evoked response (AER) · Visual evoked response (VER) · Fetal brain maturation · Magnetoencephalography (MEG)

1 Introduction

The human brain changes constantly during lifetime and shows high plasticity especially during early development. While the brain's high plasticity is advantageous concerning the rehabilitation of functions after brain damage, unfortunately it also makes the brain vulnerable to external influences, especially during prenatal brain development. In addition to the "normal" differences between age groups, external influences during fetal development can also cause alterations in brain development leading to impairments in individual cognitive processes. During the last decades, augmented research has been done concerning "fetal programming," showing that maternal stress (Talge et al. 2007), exposure to lead (Jedrychowski et al. 2009) or cocaine (Singer et al. 2008), as well as maternal undernutrition (Szitanyi et al. 2003) or obesity (Muhlhausler et al. 2008) during pregnancy can negatively influence cognitive development or increase the risk of developing diseases such as type 2 diabetes in later life.

Since human brain development is such a fragile process, which can be influenced by many different internal and external factors, evaluation of this process

especially before birth can give first indications of possible deficits. This might serve as a first step toward an even faster and more adequate treatment and therefore help in the future to decrease the risk of negative outcomes for later life. To evaluate healthy cognitive development in utero, basic research is needed. Only by knowing the developmental steps of the healthy brain, modifications from this process can be detected and treatment initiated.

The fetal magnetoencephalography (fMEG) is a noninvasive technique which enables the investigation of human brain development in utero by evaluating spontaneous fetal brain activity, fetal brain reactions to auditory or visual stimulation, and change detection between stimuli or habituation to repetitively presented stimuli. In this chapter we provide an overview of human central nervous system (CNS) development during the fetal period. Subsequently, the fMEG and its possible applications are introduced and discussed, and an overview of the current state of the art in fMEG research is given.

2 Background on Human CNS Development

Shortly after conception, the human brain starts to develop. Already after 18 days postconception, the neural plate, built of tissue developing into the human nervous system, is visible and developing to form a neural tube after 24 days. Around this time, cell proliferation starts. Due to cell division, the number of cells in the neural tube increases substantially. Once created, the cells leave their place of origin to migrate to their place of destination and align themselves with other neurons in the same area (aggregation). These processes build the foundation for the formation of different structures of the human nervous system. However, to enable the newly built brain structures to function appropriately, cells need to be connected to enable interaction between different structures. This cell connection is initiated immediately after cell aggregation and is characterized by axon growth and synapse formation. However, due to a neuronal overproduction of about 50% of neurons, a selection takes place, which seems to be related to the integrity of the associated axon and its projection. The decay of neurons takes place either actively (apoptosis) or passively (necrosis) and is regulated by neurotrophins. To ensure the appropriate function of brain structures, axons of the surviving neurons sprout to occupy gaps, which arose through death of neighboring cells. The process of neuronal development and migration is terminated at approximately 7 months of prenatal development. However, the development of the human brain is not "finished" at this point in time or at birth. In contrary, development continues postnatally and proceeds throughout late adolescence. The postnatal period is characterized by an intensified development of new synapses (synaptogenesis) and myelination and an increase in dendrite branching as well as synaptic loss. During the long period of brain development between conception and adulthood, different brain regions mature at different time points. While primary visual and auditory cortices are among the first to mature, reaching their maximal synapse density already in the seventh or eighth

postnatal month, the prefrontal cortex (PFC) is known to be one of the last brain regions to mature, reaching its maximal synapse density in the second year after birth. Similarly, myelination and synaptic loss occur first in the primary auditory and visual cortices and continue into adolescence in the PFC (Casey et al. 2000; Pinel 2003).

Historically, knowledge about brain development was originally gained through postmortem examinations; in vivo evaluations became possible with the invention of brain imaging techniques like magnetic resonance imaging (MRI) (for a review about developmental MRI studies, see Lenroot and Giedd (2006)). In the last decades, several studies used MRI to evaluate brain development in neonates and children (Huppi et al. 1998; Giedd et al. 1996; Casey et al. 2000). Examining 78 premature and mature newborns at the ages between 29 and 41 postconceptional weeks, Huppi et al. (1998) showed an increase in total brain tissue volume of 22 ml/week during that period. Accordingly, also total gray matter volume increased at approximately 15 ml/week. The highest increment was found in cortical rather than subcortical gray matter. In the first 2 years, synapse formation in the brain was found to be highest, and by the age of 2 years, the human brain reached about 75% of its adult weight. Moreover, no significant increment of cerebral or cerebellar volume could be found during the time period between 4 and 18 years of age (Giedd et al. 1996; Kretschmann et al. 1986; Casey et al. 2000).

2.1 Development of the Auditory System

Human hearing is a process that requires the cooperation of different parts including the ear, auditory nerve, thalamus, and primary auditory cortex. Only a flawless interaction of these systems enables the perception of sounds. The fetal outer ear can already be observed after 10 weeks of gestational age (GA) (Arabin and van Straaten 2006). The tympanic membrane and ring, which are the transition between the outer and the middle ear, are developed at 16 weeks GA. The adult size of the pinna is reached at about 19–20 weeks GA (Counter 2010). The three ossicles of the middle ear begin to develop between the fourth and the sixth week GA and reach their full size at a gestational age of 18 weeks (Counter 2010; Arabin and van Straaten 2006). In the inner ear, the hair cells can be detected after 14 weeks. At about 20 weeks of GA, the morphology of the cochlea is found to be already similar to the stage when its first function is detected. However, cochlear development was found to proceed after the 20th week GA and to mature around the 30–35th week GA (Pujol et al. 1991). Leaving the ear, the "sound waves" travel further to the auditory pathways, which undergo myelination between the 26th and 29th week of gestation. Nevertheless, myelination further progresses until the age of approximately 1 year after birth (Arabin and van Straaten 2006).

With a slight delay in comparison to the anatomical development of the fetal auditory system, first auditory experiences can be expected starting at the 20th week GA. Monitoring blink-startle reflexes in response to vibro-acoustic stimulation, Birnholz and Benacerraf (1983) detected first responses in fetuses between the

24th and 25th week GA; however, stable responses across the study group were found at the gestational age of 28 weeks. Using pure-tone stimulation of different frequencies, Hepper and Shahidullah (1994) found that responses to different frequencies are observable at different gestational ages. First responses have been detected for 500 Hz stimulation. For this frequency, they were detected even at an age of 19 weeks GA, and at the age of 27 weeks GA, 96% of the participating fetuses showed responses for frequencies of 250 and 500 Hz. Responses to higher frequencies showed a developmental delay with the fetuses responding to a frequency of 1000 Hz at 33 weeks GA and to a 3000 Hz tone at 35 weeks GA (Hepper and Shahidullah 1994). Similar gestational ages for the occurrence of fetal responses to external auditory stimulation have also been reported by others (Querleu et al. 1988). During the last trimester of gestation, the intensity of stimulation needed to elicit a fetal response was found to decrease, also indicating developmental progress (Hepper and Shahidullah 1994).

After birth, neonates' auditory system undergoes further development, which enables the localization of sound sources in the environment at about 2 months of age. At an age of around 6 months, localization is even possible in horizontal and vertical planes. In general, an improvement concerning the acuity of hearing as well as the discrimination of different speech sounds progresses over the first 3 years of life.

2.2 Development of the Visual System

Similar to the auditory system, the visual system consists of multiple parts which have to cooperate to enable human vision. This development starts in early fetal life and progresses through the first postnatal years. One of the first structures to develop is the physical structure of the eye (early phase of fetal life), while the different necessary neuronal structures and connections develop during later fetal and early neonatal life (Graven and Browne 2008). The development of the retina and its layers commences at around 24 weeks GA and is not finished until 2 or 3 months of postnatal life. This long period is determined by the development of the retinal substructures. While the rod receptors important for scotopic vision develop without any influence of light during the latter period of fetal life and are functional at term, the cone receptors important for photopic vision are not functional when the baby is born. Photopic vision develops during the first months of neonatal life. Other retinal cells mature during the period of 22–30 weeks GA. Moreover, random firing of retinal ganglion cells activates the growth of axons which become the optic nerve, the connection between the retina and the lateral geniculate nucleus (LGN). Also retinal amacrine cells start to fire to stimulate axon growth between the retina and the LGN as well as between the LGN and the visual cortex. Amacrine cell activity starts around the fetal age of 28–30 weeks GA and becomes more regular when development progresses. This regularization of activity is accompanied by the beginning of the first organized sleep states which are important for the configuration of ocular dominance columns in visual

cortex (Graven and Browne 2008). First fibers reaching the LGN were detected as early as 7 weeks GA (Cooper 1945). However, at this stage, the LGN is in the beginning of its development and consists of homogeneous cell arrangements, while the six-layer structure seen in mature LGN develops around the 22th week GA (Hitchcock and Hickey 1980; Cooper 1945). First connections between the LGN and the visual cortex, which is also organized in six layers, begin to evolve before the mid-gestational period (Henver 2000). Ocular dominance columns in the visual cortex are built in the last 8–10 weeks of gestation (Graven and Browne 2008).

While not all parts of the visual system are mature before birth and continue developing during the first years of neonatal life, much development takes place in the prenatal period between around 24 and 40 weeks GA. For example, scotopic vision becomes functional during the late prenatal period. Moreover, studies investigating fetal brain maturation showed reactions to light flashes as early as 28 weeks GA (Eswaran et al. 2004).

3 Introduction of the Fetal MEG

Since human brain development in utero is such a complex and fragile process, its anatomical as well as functional evaluation provides important information about healthy brain development. However, because the fetal head is covered by the maternal abdomen and not accessible from outside, the investigation of fetal brain function is accompanied with many challenges. Nevertheless, advances in the technology of brain imaging in the last decades made the evaluation of prenatal brain development possible. During this time, two brain imaging techniques have been developed, which showed promising results in the research of fetal brain development and function: functional MRI (fMRI) (Belliveau et al. 1991) and fetal magnetoencephalography (fMEG) (Blum et al. 1985). While fMRI has the advantage of high spatial resolution, it also involves many difficulties concerning fetal measurements. During an fMRI measurement, fetuses are exposed to high sound levels and magnetic fields, which mainly restrict the usage to fetuses presenting with clinical measurement indications. In contrast, the fMEG is a noninvasive technique, which makes it a suitable tool for basic research as well (Preissl et al. 2004, 2005). So far, the fMEG is mainly used to evaluate fetal heart signals and brain function as measured by fetal auditory evoked responses (AERs) elicited by tone stimulation, fetal visual evoked responses (VERs) elicited by light stimulation, and spontaneous fetal brain activity (for a review, see Preissl et al. (2004)).

The fMEG uses the same technique as the MEG but combines this technique with the special requirements needed for fetal and neonatal measurements. To ensure a good detection of the fetal heart and brain signals and enable the mother to have a comfortable position on the device, the sensor array is shaped to fit the maternal abdomen. Worldwide, only two dedicated fMEG devices – also called SARA systems (SQUID Array for Reproductive Assessment) – are operational so

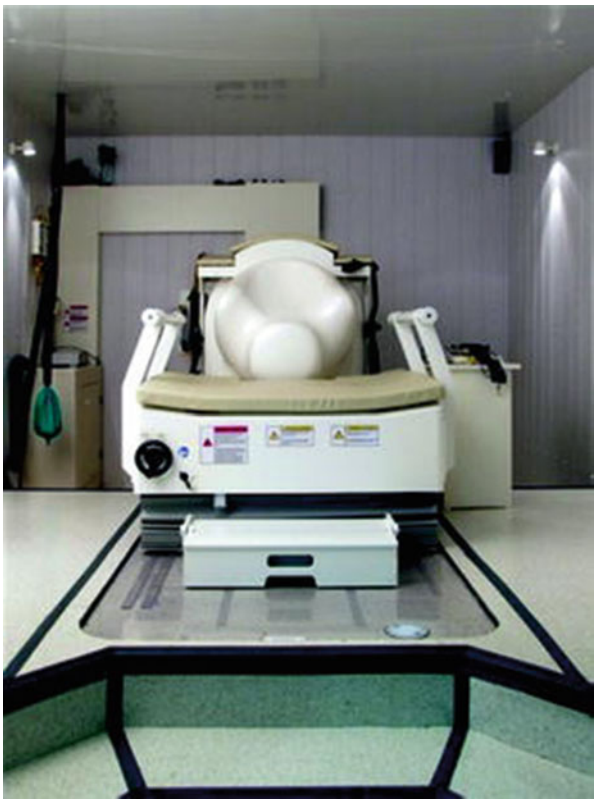

Fig. 1 156-channel fMEG device SARA II (SQUID Array for Reproductive Assessment, VSM MedTech Ltd., Port Coquitlam, Canada) installed at the fMEG Center in Tübingen. (© University Hospital Tübingen)

far. The first one was developed and installed in Little Rock, Arkansas, USA, while an advanced version was installed at the fMEG Center in Tübingen in the year 2008.

The fMEG device installed at the fMEG Center in Tübingen (SARA II, VSM MedTech Ltd., Port Coquitlam, Canada) includes 156 primary sensors and 29 reference sensors (see Fig. 1). Four localization coils are used to localize the maternal body and the fetal head in relation to the sensor array. One is attached directly to the maternal abdomen above the fetal head, one at the left and right side of the mother, respectively, and one at the maternal spine. To ensure that the measurement is not influenced by magnetic fields from the surrounding environment, the device is located within a magnetically shielded room (Vacuumschmelze, Hanau, Germany).

3.1 Fetal Measurements

Before each fetal measurement, the head position of the fetus has to be determined. Therefore, an ultrasound is performed immediately before the measurement and

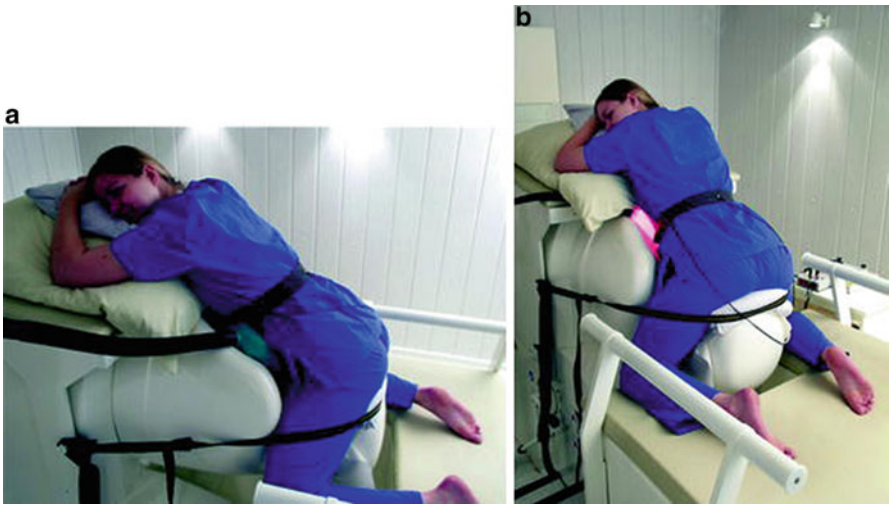

Fig. 2 Fetal measurement with (**a**) auditory and (**b**) visual stimulation. Tones are produced outside the shielded room and transmitted through air-filled tubes to a balloon located directly above the maternal abdomen. Light flashes are produced by a panel of light-emitting diodes. (© University Hospital Tübingen)

fetal head position is marked on the maternal abdomen. After finding a comfortable position on the device, localization coils are attached as described above. During the entire measurement session, contact between the subject and the researcher is ensured through a camera and an intercom. Immediately after the measurement, a second ultrasound is performed to check for changes in the fetal position.

For auditory stimulation during a measurement, stimuli are produced by loudspeakers outside the shielded room and led through air-filled tubes to a balloon which is located directly above the maternal abdomen (Fig. 2a). For visual stimulation, light stimuli are produced by a panel of light-emitting diodes (Fig. 2b).

3.2 Neonatal Measurements

For neonatal measurements, a cradle is attached to the fMEG device, which ensures that the newborn is lying comfortably and safely during the measurement. Generally, measurements are performed, while the newborn is sleeping or lying quietly.

For auditory stimulation, the newborn is lying on one side with its contralateral temporal lobe resting on the sensor array. Stimulation is produced outside the shielded room, conducted through air-filled tubes, and presented to the left ear using a headphone which is especially developed for neonatal measurements (Fig. 3). For visual stimulation, the newborn is lying on its back with its occipital lobe resting

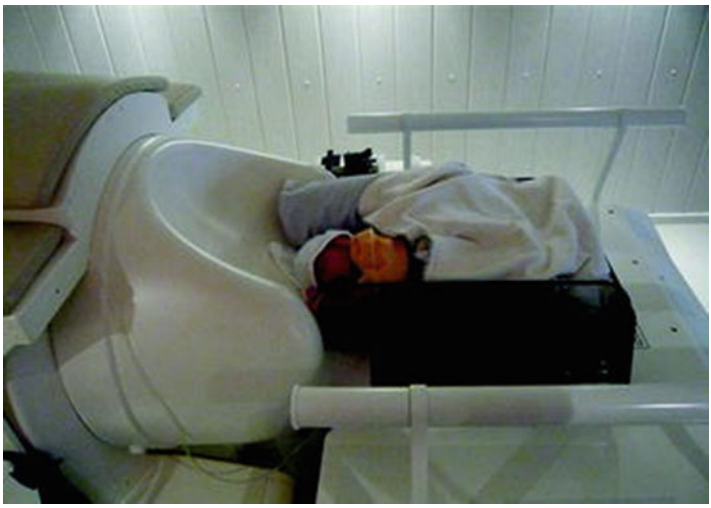

Fig. 3 Neonatal measurement with auditory stimulation. Tones are produced outside the shielded room and transmitted through air-filled tubes to small earphones especially designed for neonatal measurements. (© University Hospital Tübingen)

on the sensor array. The light pad is fixed at approximately 1 m above the neonatal head.

4 State of the Art in Functional Fetal Brain Research Using fMEG

In the year 1985, the first fetal AERs were detected using a one-channel MEG device (Blum et al. 1985). Since then, the technology was improved, and measurements with more channels were made possible. In the last decades, mainly auditory evoked responses (AERs) and visual evoked responses (VERs) were recorded, and their change over gestational age was investigated (Holst et al. 2005; Eswaran et al. 2002a, b; Schleussner and Schneider 2004). Moreover, auditory change detection (e.g., change in frequencies) was evaluated (Draganova et al. 2005, 2007), and response decrement (i.e., habituation) after repetitive auditory and visual stimulation has been investigated (Sheridan et al. 2008; Matuz et al. 2012; Muenssinger et al. 2013).

4.1 State of the Art in Auditory fMEG Research

As described above, the first human auditory experiences can be expected at 20 weeks GA. In fMEG studies using pure-tone stimulation, AERs were detected

reliably at a GA of 28 weeks (Lengle et al. 2001; Schleussner and Schneider, 2004; Eswaran et al. 2002a). While response detection rates were highly variable, an AER detection rate of around 80% could be reached in fetuses between 28 and 40 weeks GA (Schleussner and Schneider 2004; Holst et al. 2005) and 30 and 40 weeks GA (Eswaran et al. 2002a). Moreover, longitudinal studies evaluated the development of AER responses over GA. Therefore, fetuses between 27 and 40 weeks GA were included and measured at least twice with an interval of approximately 2 weeks between measurements (Holst et al. 2005). Results showed that the AER latencies decreased with increasing GA, indicating a gradual maturation of auditory processes and therefore an increase in the speed of auditory signal processing during the last trimester of pregnancy (Holst et al. 2005). These results are also in accordance with those of Schleussner and Schneider (2004), who showed decreasing latencies of the P2 pm and N2 pm components with increasing GA. These findings are first steps toward the understanding of healthy brain maturation in utero and might in the future be helpful in detecting deviant brain development. Moreover, in addition to pure sound detection, fetuses in the last trimester of pregnancy are also able to detect changes in sound frequencies (Draganova et al. 2005). To investigate this ability, an oddball paradigm was used. 500 Hz (88%) tones were intermixed with 750 Hz (12%) tones, and mismatch negativity responses (MMN), which are an indicator for change detection (in this case a change in frequency), were evaluated. It could be shown that in 48% of the fetal recordings, an MMN response was found. In a follow-up study, detection rates of MMN responses increased to 66% in fetuses between the GA of 28 and 39 weeks and 89% in newborns (Draganova et al. 2007). These results strongly indicate that the fetal brain in the last trimester of pregnancy is able to process auditory stimuli and detect changes in stimulus frequencies. This is an important prerequisite for language development and processing. Also concerning habituation, the most basic form of learning, an auditory fMEG study was performed (Muenssinger et al. 2013). Fetuses were measured using an auditory short-term habituation paradigm consisting of trains of tones including five 500 Hz tones, one 750 Hz tone (dishabituator), and another two 500 Hz tones each. After response sensitization resulting in a response increment between tones one and two, the expected response decrement for the four repetitively presented 500 Hz tones could be observed (Fig. 4).

This response decrement could either be due to sensory adaptation (fatigue) or to habituation. Therefore, not only dishabituation (response increment between last tone before and first tone after the dishabituator) but also stimulus specificity (response increment between last tone before dishabituator and dishabituator itself) were evaluated. Additionally, MMN responses between the last tone before the dishabituator (standard) and the dishabituator itself (deviant) have been investigated. Both stimulus specificity and the presence of MMN responses would be an indicator for habituation as reason for response decrement, because sensory fatigue would be stimulus independent. Significant stimulus specificity was found, and MMN responses were detected in 50% of the fetuses (Fig. 5). This indicates that already fetuses in the last trimester of pregnancy are able to show habituation, a basic form of learning.

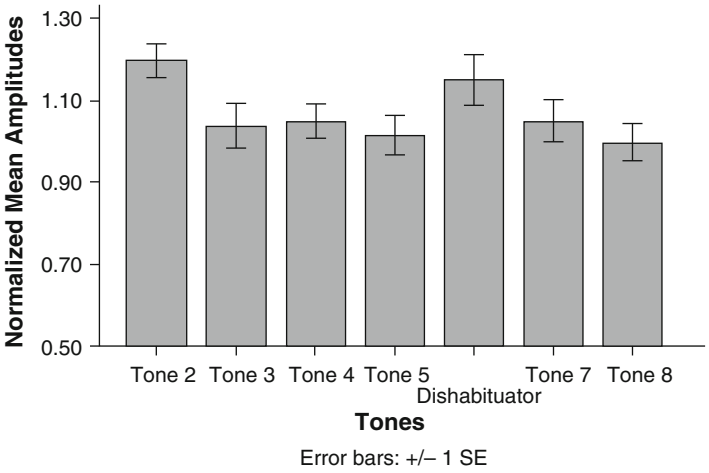

Fig. 4 Normalized fetal amplitudes to tones 2–8 of an auditory habituation paradigm. Mean and standard error are displayed. (Figure with permission from Muenssinger et al. (2013))

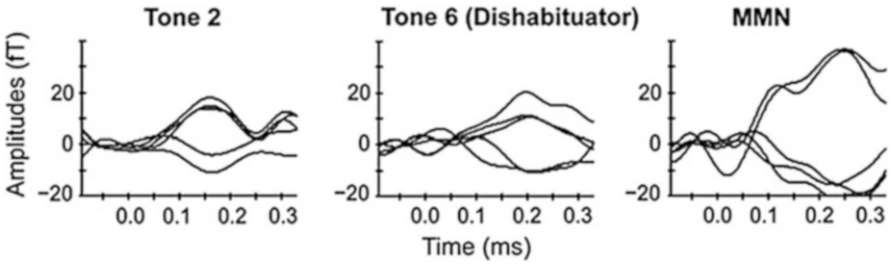

Fig. 5 Amplitude example of tone 2 and tone 6 (dishabituator) and the MMN response of one fetus at the gestational age of 36 weeks. The five channels with the highest amplitudes are shown. (Figure with permission from Muenssinger et al. (2013))

4.2 State of the Art in Visual fMEG Research

Similar to AERs, VERs have been detected in fetuses as early as in the 28th week GA. In their preliminary study, Eswaran et al. (2002b) presented 180 light flashes to 10 fetuses between the GA of 28 and 36 weeks and could show that 4 of the 10 fetuses showed evoked responses to the light stimulation. Using longer stimulus durations, the response rates could be strongly enhanced. By presenting light flashes with a duration of 100 ms or 500 ms to fetuses starting at 28 weeks GA, a response detection rate of 60% was found in fetuses between 28 and 32 weeks GA, and even a response detection rate of 70% was found in fetuses between 32 and 36 weeks GA. In the oldest fetuses (36–40 weeks GA), the response detection rate was rather low (28%). However, different than in responders, it was reported that the position of most of the non-responders was in a way that the eyes were not visible with

ultrasound which means that they were turned away from the visual stimulation. Concerning the development of VERs in fetuses over GA, it could be shown that the latencies of the fP200 component decreased with increasing GA. No changes for GA were found for the fP300 component (Eswaran et al. 2004). These results show the possibility to use fMEG to monitor fetal brain development not only using auditory stimulation but also using visual stimulation (Fig. 6).

However, for a clinical setting, the response detection rates are still not high enough. By combining both stimulation types (i.e., by presenting auditory as well as visual stimulation to the fetus), the response detection rate could be enhanced to 91% (criteria that the fetus showed a response to either one of the stimuli) (Eswaran et al. 2005). In addition to the development of stimulus processing, also studies concerning habituation have been performed using fMEG. Sheridan et al. (2008) investigated the decrement of VERs elicited by trains of four light flashes in fetuses between the GA of 29 and 37 weeks as well as in newborns between 6 and 22 days of age. Newborns showed response decrement from the first to the last light flash. In fetal recordings the response rate was low (29%), which may be caused by the low signal to noise ratio of visual evoked responses. However, for the fetuses who showed responses, either a decrement from flash one to two or a response for flash one followed by no detectable response for the following flashes was detected. This might at least indicate that response decrement to visual stimuli can be detected in utero. Similar results have also been shown by Matuz et al. (2012), who presented four light flashes to fetuses and neonates but also included an auditory dishabituator in the trains of light stimuli, which was presented after the fourth light flash. Neonatal results showed response decrement between the first and the last light flash as well as response recovery for the dishabituator. For fetal measurements, a low detection rate was found, but a decrement between the VER of flashes one and two could be detected in those fetuses showing VERs. These two studies indicate that newborns born at term show visual response decrement as well as response recovery when an array of repetitive stimuli is interrupted by a novel stimulus. Moreover, there are first indications that already the fetal brain might be capable of showing visual habituation. However, further research is needed to clearly show visual response decrement in utero and to gain more information about the question if visual response decrement is due to habituation, a basic form of learning, or sensory adaptation/fatigue.

4.3 State of the Art in Clinical fMEG Research Using Auditory and Visual Stimulation

The knowledge obtained from fMEG research with healthy fetuses and neonates was used to assess clinical questions. In utero, there are different factors which can influence fetal brain maturation. Intrauterine growth restriction (IUGR) is one factor known to increase the risk for neurologic damage due to oxygen deprivation of the fetal brain as a consequence of placental insufficiency. Therefore, the developmental course of IUGR fetuses is expected to be delayed. Kiefer et al. (2008) used fMEG

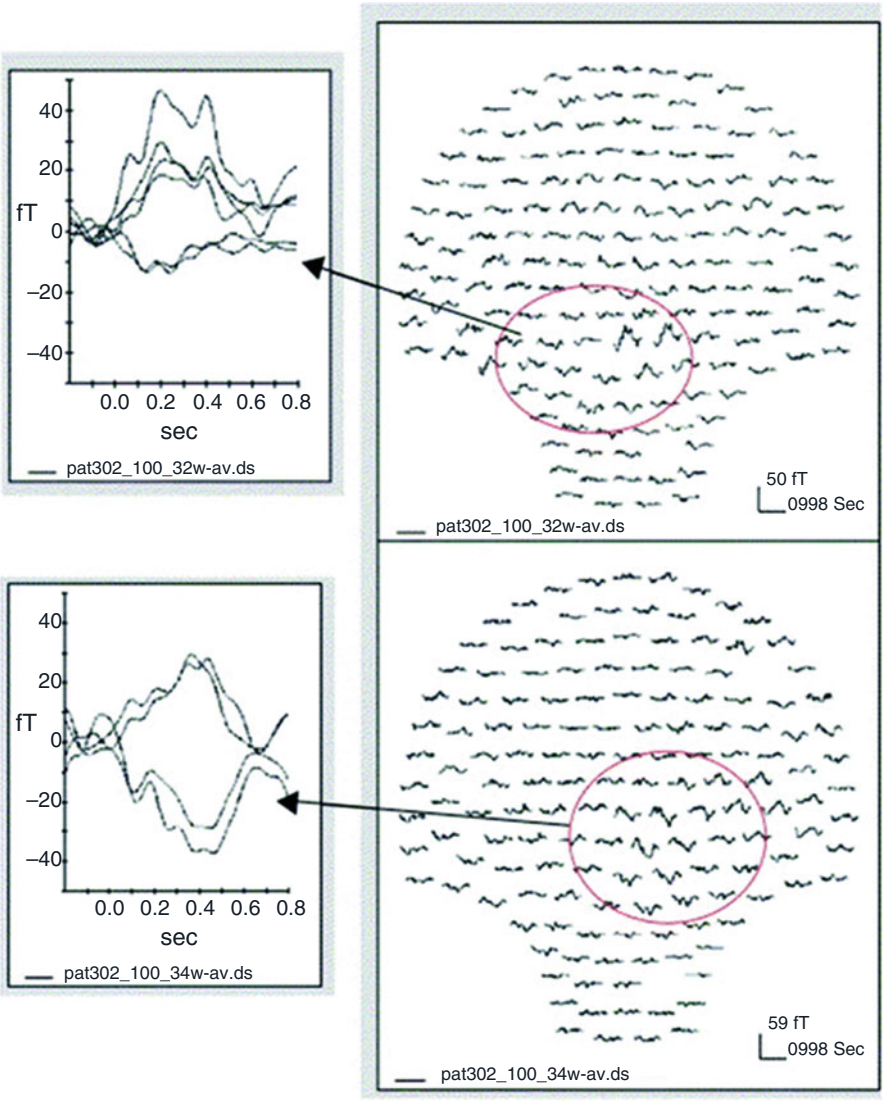

Fig. 6 Averaged VER responses and their locations on the 151 sensor array map from a fetus at 32 (*top*) and 34 (*bottom*) weeks of gestation. The flash duration was 100 ms. (Figure with permission from Eswaran et al. (2004))

to investigate fetal brain maturation in fetuses (≥27 weeks GA) who were small for gestational age (SGA), a state defined by a weight below the 10th percentile of the GA age group. In this group, placental insufficiency was expected and validated in 12 of 14 cases through the use of Doppler scans. Results of the SGA group were compared to results of a group of healthy fetuses to assess possible

delays in stimulus processing. Both groups were presented with tone burst and AER latencies were evaluated. Results showed longer AER latencies for the group of SGA fetuses in comparison to the group of healthy fetuses. In line with prior studies (Schleussner and Schneider 2004; Holst et al. 2005), a decrement of AER latencies with increasing GA was found in both groups. These fMEG results are a strong indicator for delayed brain maturation in SGA fetuses.

Another factor which may influence fetal brain development is the administration of medication to the mother. Steroids are often administered to the mother to induce fetal lung maturation if premature birth is suspected. However, animal models showed that antenatal steroids involve a delay in fetal brain myelination as well as a delay in fetal brain growth (Whitelaw and Thoresen 2000). Schneider et al. (2011) investigated the fetuses of mothers who received a steroid treatment for medical reasons. Steroids were given at 2 consecutive days, and fMEG measurements were conducted before the first as well as not later than 3 h after the second administration. All fetuses were presented with pure-tone stimulation. Results showed a delay in AER responses after steroid administration. Even though steroid administration has been proven to be lifesaving, the results of this study emphasize that they should only be administered when the benefits outweigh the risks.

5 Summary

In the last decades, fMEG opened a new possibility to investigate fetal functional brain development by enabling the direct evaluation of fetal brain responses to different kinds of stimulation. Since the fetal brain is especially vulnerable to internal as well as external influences during that period, knowledge about healthy brain development in utero is needed. Only by knowing how the healthy brain develops, it is possible to detect deviations or delays. Early detection of developmental deviation or delays could enable faster postnatal treatment and therefore improve treatment outcome. Moreover, by examining the harmful effects to the fetus which are induced by maternal medication, the advantages and disadvantages of drug administration can be better weighted, which in turn could also decrease negative neonatal outcomes. Taken together, the fMEG is a promising tool to investigate functional brain development in utero.

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